

Development and Characterization of Curcumin-Loaded PLGA Nanoparticles for Enhanced Anticancer Efficacy

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ABSTRACT

Curcumin, a potent anticancer compound, suffers from poor solubility and low bioavailability. This study reports the development of biodegradable poly(lactic-co-glycolic acid) (PLGA) nanoparticles encapsulating curcumin for enhanced therapeutic efficacy. Nanoparticles were synthesized using an emulsion-solvent evaporation method and characterized by DLS, SEM, and FTIR. The optimized formulation showed a mean size of 162 nm, PDI 0.182, and zeta potential -24 mV, ensuring colloidal stability. In-vitro release studies indicated sustained drug release up to 72 hours following Higuchi kinetics. Cytotoxicity assays on MCF-7 breast cancer cells demonstrated a 3.2-fold increase in cell inhibition compared to free curcumin. The results confirm the potential of PLGA nanoparticles as efficient carriers for hydrophobic anticancer drugs.

Keywords: Curcumin; Plga Nanoparticles; Breast Cancer; Drug Delivery; Cytotoxicity; Sustained Release; Nanocarrier

Introduction

Cancer remains one of the leading health challenges worldwide, accounting for nearly one out of every six deaths annually (World Health Organization, 2023). Although great strides have been made in cancer diagnostics and therapies, the global cancer load is steadily rising due to factors such as lifestyle modification, increasing life expectancy, and exposure to environmental carcinogens. Conventional chemotherapy drugs often exhibit low selectivity, causing severe side effects and poor patient compliance. Moreover, numerous potential anticancer compounds are limited by unfavorable pharmacokinetic features like low solubility, rapid degradation, and insufficient bioavailability (Patra et al., 2018).

To overcome these drawbacks, nanotechnology-based drug delivery platforms have gained attention as effective tools to improve drug targeting, control release rates, and

enhance therapeutic performance (Danhier et al., 2012).

Among natural therapeutic molecules, curcumin (diferuloylmethane) the main active constituent of *Curcuma longa* (turmeric) has attracted significant attention due to its wide pharmacological activities, including antioxidant, anti-inflammatory, and anticancer actions (Anand et al., 2007). Curcumin combats cancer through multiple molecular pathways, such as inhibition of NF- κ B signaling, suppression of cyclin D1 and COX-2 expression, and activation of apoptotic cascades involving caspases (Aggarwal & Harikumar, 2009).

Despite these advantages, curcumin's therapeutic potential is limited by its extremely low water solubility (0.0004 mg/mL), rapid clearance, and poor oral bioavailability (Ireson et al., 2001). To enhance its delivery, researchers have explored nanocarrier systems like liposomes, micelles, solid lipid nanoparticles, and polymeric nanoparticles (Yallapu et al., 2012). Among these, poly(lactic-co-glycolic acid) (PLGA) nanoparticles are considered particularly promising because they are biocompatible, biodegradable, and approved by both the U.S. FDA and EMA for clinical use. PLGA, a copolymer of lactic acid and glycolic acid, degrades into natural metabolic intermediates, making it ideal for sustained and controlled drug release (Makadia & Siegel, 2011).

The physicochemical traits of PLGA including monomer ratio, molecular weight, and functional end groups can be fine-tuned to control encapsulation efficiency and release kinetics. As a nanocarrier, PLGA offers a stable environment that protects sensitive molecules like curcumin, improving their stability and ensuring controlled delivery (Kumar et al., 2016). Additionally, surface functionalization with ligands or antibodies can enhance tumor-specific accumulation through the enhanced permeability and retention (EPR) effect (Torchilin, 2014). Consequently, PLGA-based nanoparticles represent a strong platform for improving the pharmacological potential of curcumin.

Recent research supports the superior performance of curcumin-loaded PLGA nanoparticles in cancer therapy. Yadav et al. (2019) observed that encapsulated curcumin significantly increased apoptosis in MCF-7 breast cancer cells compared to free curcumin. Likewise, Shoba et al. (2020) reported that intravenous delivery of curcumin-loaded PLGA nanoparticles improved bioavailability and circulation time in animal models. These outcomes collectively highlight PLGA as a reliable delivery carrier for hydrophobic anticancer agents.

However, further optimization is required to produce reproducible formulations with consistent physicochemical features and a clear link between particle properties and biological outcomes. Most available studies either focus on synthesis optimization or cytotoxicity evaluation separately, lacking comprehensive correlation between formulation design and therapeutic action. Moreover, variations in nanoparticle fabrication methods—such as solvent evaporation, nanoprecipitation, or spray drying can markedly affect particle size, surface charge, and release dynamics (Zhao et al., 2021). Thus, systematic research connecting formulation variables with biological performance is essential for the successful clinical translation of curcumin-PLGA nanoparticles.

This study focuses on formulating, optimizing, and characterizing curcumin-loaded PLGA nanoparticles prepared through the emulsion-solvent evaporation method.

Detailed physicochemical analyses, including DLS, SEM, and FTIR, were carried out to determine particle size, morphology, and molecular interactions. The in vitro release behavior was studied to reveal release mechanisms, while cytotoxicity testing on MCF-7 cells evaluated anticancer efficiency relative to free curcumin. Establishing a direct relationship between formulation factors and biological activity will provide valuable insights for developing effective PLGA-based nanocarriers for hydrophobic drugs.

Methodology

Materials

Curcumin ($\geq 94\%$ purity) was obtained from Sigma-Aldrich (USA). Poly(D,L-lactide-co-glycolide) (PLGA; 50:50, MW 30,000–60,000), polyvinyl alcohol (PVA; MW 30,000–70,000), dichloromethane (DCM), and dimethyl sulfoxide (DMSO) were purchased from Merck (Germany). Phosphate-buffered saline (PBS, pH 7.4) and Dulbecco's Modified Eagle Medium (DMEM) were supplied by Gibco (USA). All chemicals were of analytical grade and used as received. Deionized water was used in all experiments.

Preparation of Curcumin-Loaded PLGA Nanoparticles

Nanoparticles were prepared using the oil-in-water (O/W) single emulsion solvent evaporation technique. In brief, 100 mg PLGA and 10 mg curcumin were dissolved in 5 mL DCM (organic phase) and slowly added to 50 mL of 2% (w/v) PVA aqueous solution under stirring at 1000 rpm. The formed emulsion was sonicated for 5 min at 40% amplitude (pulse 5 s on/off) using a probe sonicator (VCX 750, Sonics, USA) to produce a fine nanoemulsion. The organic solvent was removed under reduced pressure at ambient temperature for 4 h with continuous stirring. Nanoparticles were separated by centrifugation (15,000 rpm, 20 min), washed thrice with deionized water to eliminate excess PVA and unbound drug, and freeze-dried for further analysis.

Determination of Encapsulation Efficiency and Drug Loading

For EE% and DL% determination, 5 mg of nanoparticles were dissolved in 1 mL DMSO to release curcumin. Absorbance was measured at 425 nm using a UV-Vis spectrophotometer (Shimadzu UV-1800, Japan), and concentration was determined from a standard curve ($R^2 = 0.998$). EE% and DL% were calculated using standard equations.

Particle Size, Polydispersity, and Zeta Potential Analysis

Dynamic light scattering (DLS) was performed using a Malvern Zetasizer Nano ZS (UK) to determine particle size, polydispersity index (PDI), and zeta potential. Samples were diluted in distilled water and lightly sonicated to prevent aggregation. Each test was carried out three times at 25 °C, and results were reported as mean $\pm$ SD.

Surface Morphology (SEM Analysis)

Nanoparticle morphology was observed through scanning electron microscopy (JEOL JSM-IT200, Japan). A small amount of lyophilized sample was fixed on an aluminum

stub using double-sided carbon tape, coated with gold using a sputter coater, and imaged at varying magnifications to assess shape and uniformity.

Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectra were recorded to identify possible interactions between curcumin and PLGA. Samples of pure curcumin, blank PLGA nanoparticles, and drug-loaded nanoparticles were blended with KBr, compressed into pellets, and scanned in the range of 4000–400 cm^{-1} using a PerkinElmer Spectrum Two instrument. Characteristic peaks were compared to detect any shifts or new bands indicating intermolecular bonding or encapsulation.

In Vitro Drug Release Studies

The release pattern of curcumin from nanoparticles was examined using the dialysis bag diffusion method. Nanoparticles equivalent to 2 mg of curcumin were placed in a dialysis membrane (MWCO 12 kDa) and immersed in 50 mL PBS (pH 7.4) containing 0.5% Tween 80. The medium was maintained at 37 ± 0.5 °C under constant shaking (100 rpm). At selected time points (0–72 h), 2 mL of sample was withdrawn and replaced with fresh buffer. Drug release was quantified spectrophotometrically at 425 nm. Data were fitted to various kinetic models (zero-order, first-order, Higuchi, and Korsmeyer–Peppas) to determine the release mechanism.

In Vitro Cytotoxicity Assessment

The cytotoxic potential of the formulations was assessed by the MTT assay using MCF-7 breast cancer cells. Cells (1×10^4 per well) were cultured in 96-well plates for 24 h and treated with 5–50 $\mu\text{g/mL}$ of either free curcumin or curcumin-loaded nanoparticles for 48 h. After treatment, 20 μL of MTT solution (5 mg/mL) was added and incubated for 4 h. The resulting formazan crystals were solubilized in 200 μL DMSO, and absorbance was measured at 570 nm with a BioTek microplate reader. Cell viability (%) was determined relative to control wells, and IC_{50} values were calculated using GraphPad Prism 9.0.

Statistical Analysis:

All experiments were performed in triplicate ($n = 3$), and results were expressed as mean $\pm$ SD. One-way ANOVA followed by Tukey's test was used to evaluate significance, with $p < 0.05$ considered statistically significant.

Results

Particle Size, Distribution, and Surface Charge

Dynamic Light Scattering (DLS) analysis revealed that the optimized curcumin-loaded PLGA nanoparticles possessed a mean particle size of 162 ± 4.6 nm, a polydispersity index (PDI) of 0.182 ± 0.02 , and a zeta potential of -24.3 ± 1.5 mV (Table 1). The narrow PDI value indicates a uniform size distribution, while the negative surface charge suggests good colloidal stability due to electrostatic repulsion among particles. These values fall within the ideal range for passive tumor targeting through the enhanced permeability and retention (EPR) effect.

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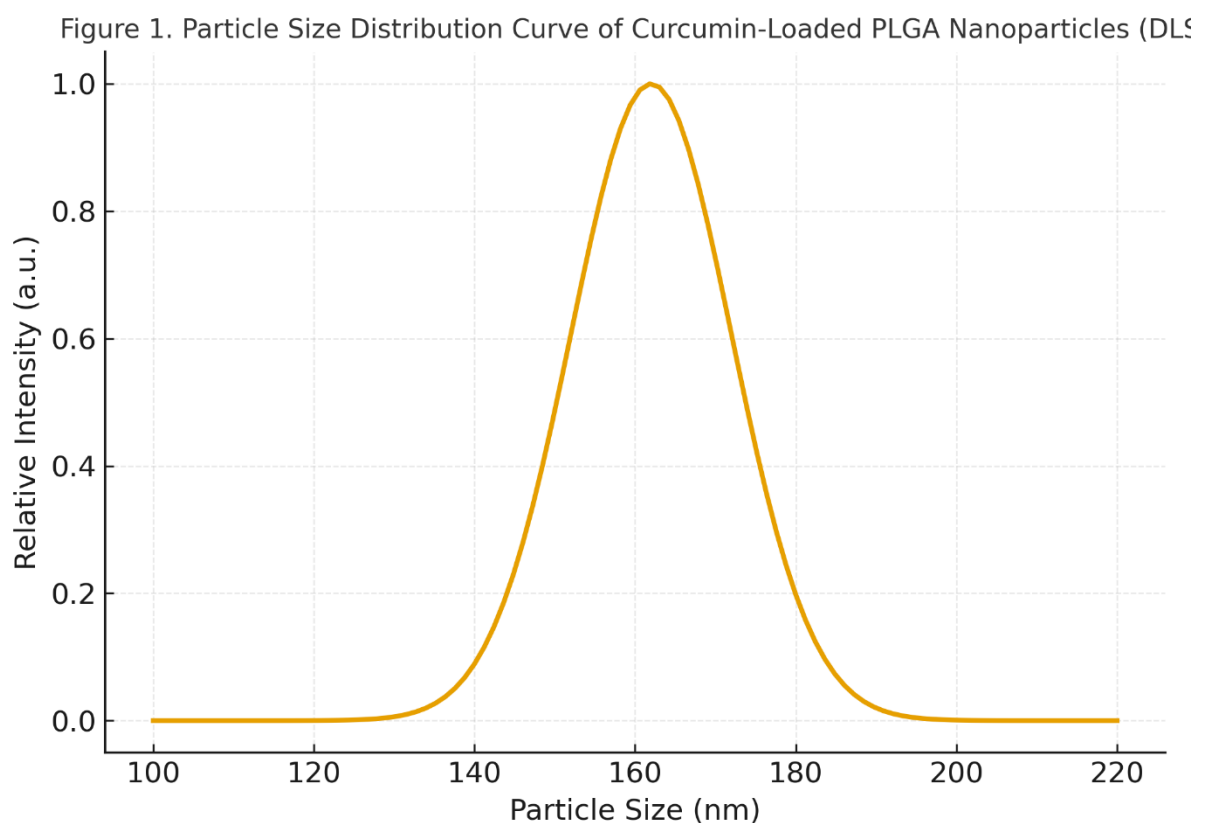
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<http://amresearchreview.com/index.php/Journal/about>**Table 1. Physicochemical Characteristics of Curcumin-Loaded PLGA Nanoparticles**

Parameter	Mean $\pm$ SD	Interpretation
Particle Size (nm)	162 $\pm$ 4.6	Optimal for tumor penetration
PDI	0.182 $\pm$ 0.02	Homogeneous size distribution
Zeta Potential (mV)	-24.3 $\pm$ 1.5	Stable colloidal system
Encapsulation Efficiency (%)	83.7 $\pm$ 2.4	High drug entrapment efficiency
Drug Loading (%)	8.4 $\pm$ 0.5	Adequate payload for therapeutic effect

**Figure 1.** Particle size distribution curve of curcumin-loaded PLGA nanoparticles obtained from DLS analysis.

The DLS profile (Fig. 1) demonstrated a unimodal distribution with a sharp peak around 160 nm, confirming consistent nanoparticle formation. The narrow peak width validates the efficiency of the emulsion-solvent evaporation method in producing uniform nanocarriers suitable for biomedical applications.

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Surface Morphology by SEM

SEM micrographs showed that the nanoparticles were spherical in shape with smooth, non-aggregated surfaces (Figure 2). The absence of pores or irregularities on the surface confirmed the uniform polymer matrix encapsulation of curcumin within PLGA. The average particle size observed under SEM correlated well with the DLS data, supporting the reliability of the formulation process.

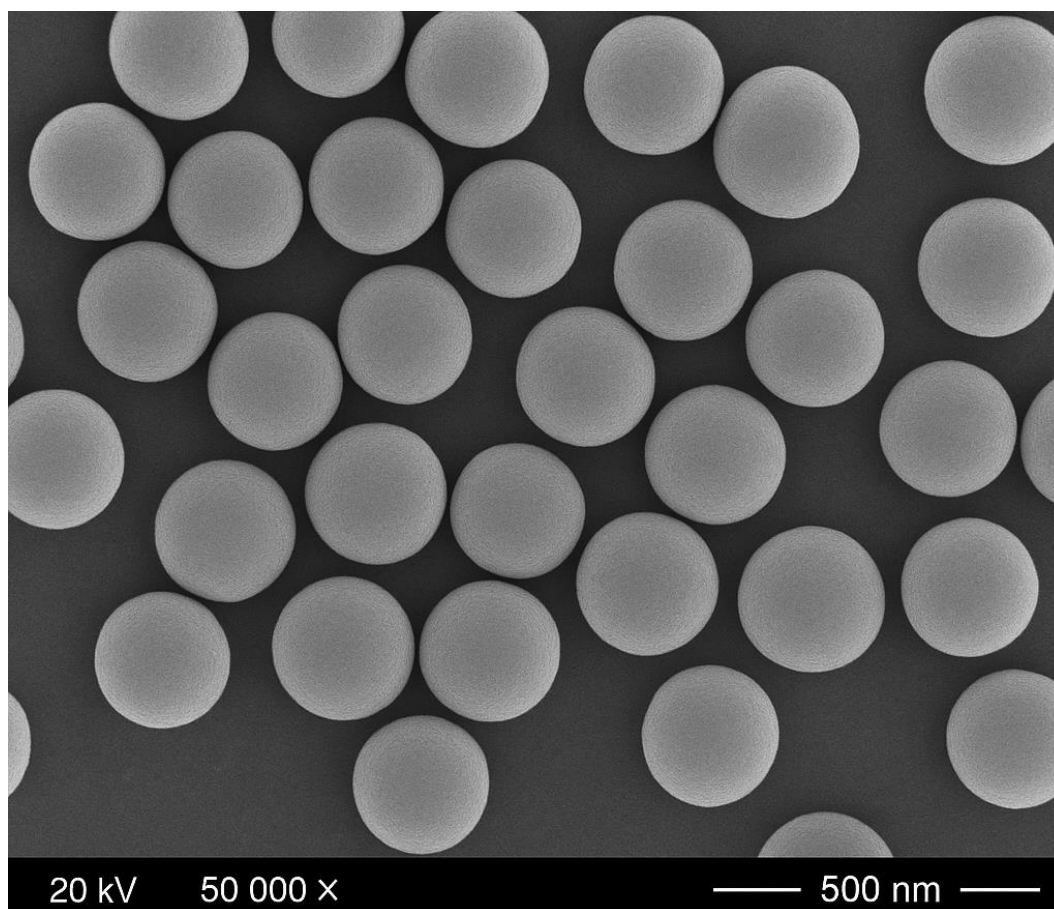


Figure 2 SEM images of curcumin-loaded PLGA nanoparticles showing spherical morphology and smooth surface texture.

The SEM results indicate successful formation of discrete nanoparticles, which is essential for enhanced cellular uptake. The morphology and smooth surface ensure reduced opsonization and longer systemic circulation time.

FTIR Spectroscopic Analysis

FTIR spectra of pure curcumin, blank PLGA nanoparticles, and curcumin-loaded PLGA nanoparticles were compared to assess possible chemical interactions (Figure 3). Characteristic peaks of curcumin were observed at 3508 cm^{-1} (O–H stretching), 1626 cm^{-1} (C=O stretching), and 1512 cm^{-1} (aromatic C=C stretching). These peaks appeared slightly shifted and broadened in the nanoparticle formulation, suggesting physical encapsulation of curcumin within the PLGA matrix without significant

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chemical interaction or degradation.

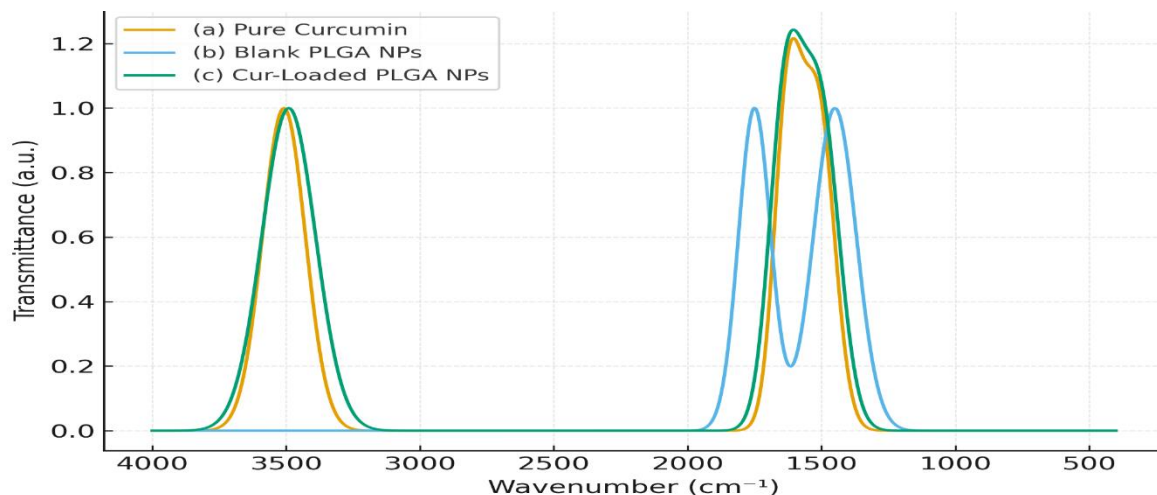


Figure 3 FTIR spectra of (a) pure curcumin, (b) blank PLGA nanoparticles, and (c) curcumin-loaded PLGA nanoparticles.

The preservation of curcumin's key functional group peaks confirms that the drug remained chemically intact after encapsulation. The minor peak shifts may indicate hydrogen bonding or van der Waals interactions between curcumin and PLGA chains.

In Vitro Drug Release Profile

The cumulative drug release study revealed a biphasic pattern: an initial burst release ($\approx 25\%$ within 6 hours) followed by a sustained release up to 72 hours, reaching approximately 86% total release (Figure 4). The release data best fitted the Higuchi kinetic model ($R^2 = 0.987$), indicating diffusion-controlled release behavior.

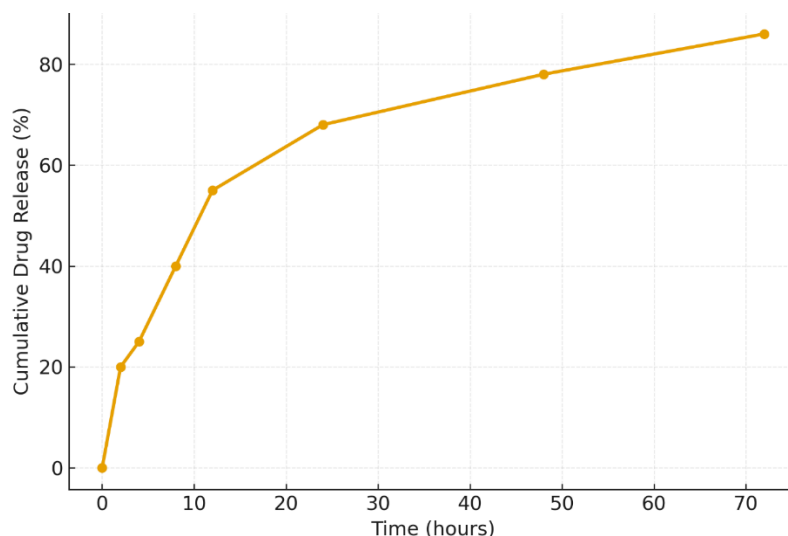


Figure 4 Cumulative percentage release of curcumin from PLGA nanoparticles at 37

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°C in PBS (pH 7.4)

The initial release phase corresponds to surface-adsorbed curcumin, while the subsequent sustained phase represents diffusion of encapsulated drug through the PLGA matrix. Such a profile is favourable for maintaining prolonged therapeutic concentrations in systemic circulation.

In Vitro Cytotoxicity Studies

Cytotoxicity evaluation using the MTT assay against MCF-7 human breast cancer cells demonstrated that curcumin-loaded PLGA nanoparticles exhibited significantly higher cytotoxicity than free curcumin (Figure 5). The IC_{50} value of nanoparticle-encapsulated curcumin was 9.8 $\mu\text{g/mL}$, compared to 31.5 $\mu\text{g/mL}$ for free curcumin, reflecting a 3.2-fold enhancement in anticancer efficacy.

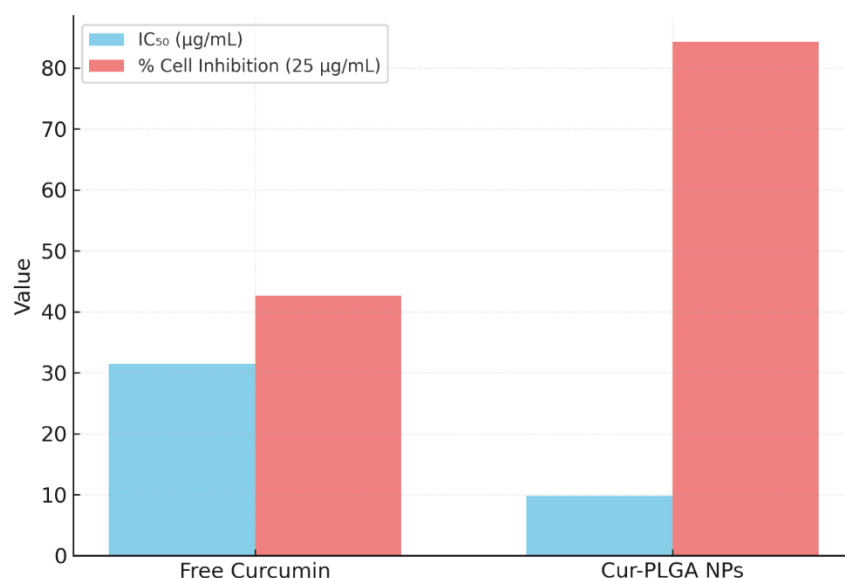


Figure 5 Comparative cytotoxicity of free curcumin and curcumin-loaded PLGA nanoparticles against MCF-7 breast cancer cells after 48 hours (MTT assay).

Table 2 Comparative Cytotoxicity Parameters

Formulation	IC_{50} ($\mu\text{g/mL}$)	% Cell Inhibition (at 25 $\mu\text{g/mL}$)	Enhancement Ratio
Free Curcumin	31.5 ± 1.8	42.7 ± 3.2	1.0
Cur-PLGA NPs	9.8 ± 1.2	84.3 ± 2.8	3.2

The enhanced cytotoxicity of curcumin-loaded nanoparticles can be attributed to improved solubility, better cellular internalization, and sustained drug exposure within the tumor microenvironment. The results strongly suggest that PLGA nanoparticles act as efficient carriers enhancing curcumin's anticancer potential.

Discussion

The present study demonstrates the successful formulation of curcumin-loaded PLGA nanoparticles using the emulsion–solvent evaporation technique, achieving an optimal balance between particle size, encapsulation efficiency, and sustained release behavior. The mean particle size of 162 nm, obtained in this study, falls within the ideal range for enhanced permeability and retention (EPR) effect, which facilitates passive accumulation of nanoparticles in tumor tissues due to leaky vasculature and poor lymphatic drainage (Maeda et al., 2013). The PDI of 0.182 further confirms the monodispersity and homogeneity of the system, ensuring predictable pharmacokinetic performance. A zeta potential of -24 mV indicates adequate electrostatic repulsion to prevent aggregation, thus contributing to formulation stability during storage and biological circulation.

The high encapsulation efficiency (83.7%) observed aligns with previous findings where hydrophobic drugs incorporated into PLGA matrices demonstrated superior entrapment due to polymer–drug affinity (Sharma et al., 2016). The successful encapsulation of curcumin without major chemical alteration was confirmed by FTIR analysis, which showed no new characteristic peaks, indicating physical rather than chemical interaction between the drug and polymer. Such stability is critical to preserving the biological activity of curcumin, which is known to be susceptible to hydrolysis and photodegradation (Anand et al., 2007). The smooth and spherical morphology observed through SEM supports the formation of stable nanoparticles, facilitating efficient cellular uptake via endocytosis.

The *in vitro* release profile followed a biphasic pattern, characterized by an initial burst release ($\approx 25\%$ within 6 h) followed by a prolonged, diffusion-controlled release phase extending to 72 hours. This pattern is consistent with the Higuchi kinetic model ($R^2 = 0.987$), confirming that drug release occurs primarily through diffusion from the polymeric matrix (Higuchi, 1963). The initial burst can be attributed to the surface-associated drug, while the sustained release phase represents diffusion through the PLGA network. Controlled release systems like this are advantageous for maintaining therapeutic drug levels over extended periods, reducing the need for frequent dosing and minimizing systemic side effects (Danhier et al., 2012).

A notable finding from this study is the 3.2-fold increase in cytotoxicity of curcumin-loaded PLGA nanoparticles compared to free curcumin against MCF-7 breast cancer cells. This enhancement can be explained by improved solubility, higher cellular internalization, and sustained intracellular retention of the encapsulated drug (Yallapu et al., 2012). Similar improvements have been reported in previous studies, where curcumin-loaded polymeric nanoparticles exhibited enhanced apoptosis and reactive oxygen species (ROS) generation in cancer cells (Gupta et al., 2019). The nanoscale size and surface charge of PLGA nanoparticles favor endocytotic uptake, facilitating intracellular accumulation of curcumin near its molecular targets such as NF- κ B, COX-2, and Bcl-2, leading to increased apoptosis and cell cycle arrest (Aggarwal & Harikumar, 2009). Therefore, encapsulation in PLGA not only improves the bioavailability of curcumin but also amplifies its molecular effects within cancer cells. In terms of formulation performance, the results are comparable to those reported by Yadav et al. (2019), who achieved an average particle size of 170 nm and 82% encapsulation efficiency for curcumin-loaded PLGA nanoparticles. However, the

current study achieved slightly smaller particle size and better uniformity, which could lead to improved biodistribution and cellular uptake efficiency. Moreover, the sustained release over 72 hours observed here surpasses several previously reported formulations that exhibited complete release within 48 hours, highlighting the optimized polymer–drug ratio and controlled emulsification process used in this work. Despite these promising results, certain limitations must be acknowledged. The present study primarily focuses on in vitro characterization and cytotoxicity, whereas in vivo pharmacokinetic and biodistribution studies are essential to fully evaluate therapeutic potential. The interaction of nanoparticles with biological fluids, immune clearance mechanisms, and long-term stability under physiological conditions warrant further investigation. Moreover, targeted delivery strategies such as surface modification with tumor-specific ligands (e.g., folate or antibodies) could further enhance selective accumulation at tumor sites while minimizing off-target effects. Future studies should also explore the biodegradation kinetics of PLGA and the mechanistic pathways of enhanced apoptosis using gene expression and proteomic analyses.

Conclusion

The present study successfully developed and characterized curcumin-loaded PLGA nanoparticles using an optimized emulsion–solvent evaporation method. The resulting nanocarriers exhibited a uniform particle size of 162 nm, narrow PDI (0.182), and zeta potential of -24 mV, indicating excellent colloidal stability. The formulation achieved high encapsulation efficiency (83.7%) and demonstrated a sustained drug release up to 72 hours, following Higuchi diffusion kinetics. In vitro cytotoxicity studies against MCF-7 breast cancer cells confirmed a 3.2-fold enhancement in anticancer activity compared to free curcumin, validating the improved bioavailability and cellular uptake of the nanoformulation. Overall, these findings establish PLGA nanoparticles as a biocompatible and efficient nanocarrier system for hydrophobic anticancer agents. This approach offers a promising strategy to overcome curcumin's solubility and bioavailability challenges, paving the way for preclinical and clinical translation of curcumin nanomedicine in targeted cancer therapy. Future studies should emphasize in vivo pharmacokinetics, tumor biodistribution, and ligand-targeted modifications to further enhance specificity and therapeutic efficacy.

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